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Supplemental Material

The Association of Prenatal Exposure to Perfluorinated Chemicals with Glucocorticoid and Androgenic Hormones in Cord Blood Samples: The Hokkaido Study

Houman Goudarzi, Atsuko Araki, Sachiko Itoh, Seiko Sasaki, Chihiro Miyashita, Takahiko Mitsui, Hiroyuki Nakazawa, Katsuya Nonomura, and Reiko Kishi

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Table S1. Correlations between cord blood glucocorticoid and androgenic hormones
(n=185)

	Cortisol		Cortisone		DHEA		Androstene-dione	
	ρ^*	p-value	ρ	p-value	ρ	p-value	ρ	p-value
Cortisol	1							
Cortisone	0.641	<0.001	1					
DHEA	-0.204	0.005	-0.301	<0.001	1			
Androstenedione	0.113	0.123	0.154	0.035	0.329	<0.001	1	

* ρ : Spearman Rho

Table S2. Association of prenatal PFC levels and cord blood cortisol and cortisone by sex stratification.

	PFOS			PFOA		
	β	(95% CI)	p-value	β	(95% CI)	p-value
Boys (n=81)						
Cortisol						
Crude	-0.237	(-1.27, -0.056)	0.032	0.141	(-0.176, 0.803)	0.206
Adjusted ^a	-0.262	(-1.39, -0.071)	0.030	0.195	(-0.177, 1.04)	0.162
Cortisone						
Crude	-0.308	(-1.90, -0.349)	0.005	0.084	(-0.400, 0.890)	0.452
Adjusted ^a	-0.291	(-1.92, -0.204)	0.016	0.210	(-0.164, 1.42)	0.118
Girls (n=104)						
Cortisol						
Crude	-0.279	(-1.46, -0.284)	0.004	0.088	(-0.234, 0.624)	0.369
Adjusted ^a	-0.326	(-1.76, -0.282)	0.007	0.095	(-0.280, 0.700)	0.397
Cortisone						
Crude	-0.283	(-2.02, -0.409)	0.003	0.055	(-0.422, 0.757)	0.574
Adjusted ^a	-0.309	(-2.36, -0.289)	0.012	0.104	(-0.368, 0.998)	0.362

^a Fully adjusted for gestational age, maternal age, parity, smoking and caffeine intake during pregnancy, maternal educational level, and blood sampling period.

Both exposure and outcome measures were log₁₀ transformed.

Table S3. Association of prenatal PFC levels with cord blood DHEA, and androstenedione by sex stratification.

	PFOS			PFOA		
	β	(95% CI)	p-value	β	(95% CI)	p-value
Boys (n=81)						
DHEA						
Crude	0.290	(0.106, 0.701)	0.008	-0.148	(-0.406, 0.080)	0.185
Adjusted ^a	0.308	(0.099, 0.755)	0.011	-0.312	(-0.642, -0.043)	0.025
Androstenedione						
Crude	-0.092	(-0.390, 0.161)	0.410	-0.193	(-0.404, 0.026)	0.084
Adjusted ^a	-0.011	(-0.312, 0.284)	0.926	-0.230	(-0.490, 0.038)	0.093
Girls (n=104)						
DHEA						
Crude	0.232	(0.068, 0.694)	0.017	-0.091	(-0.329, 0.199)	0.354
Adjusted ^a	0.238	(-0.016, 0.796)	0.059	-0.170	(-0.457, 0.065)	0.140
Androstenedione						
Crude	0.004	(-0.224, 0.236)	0.960	-0.073	(-0.221, 0.100)	0.460
Adjusted ^a	0.004	(-0.290, 0.300)	0.972	-0.096	(-0.267, 0.109)	0.406

^a Fully adjusted for gestational age, maternal age, parity, smoking and caffeine intake during pregnancy, maternal educational level, and blood sampling period.
Both exposure and outcome measures were log₁₀ transformed.

Table S4. Adjusted^a least square means (LSM) and regression coefficients (β) for glucocorticoid and androgenic hormones in cord blood samples by quartiles of PFCs (n=185).

	Adjusted ^a	Cortisol			Adjusted ^a	Cortisone			Adjusted ^a	DHEA			Adjusted ^a	Androstenedione		
	LSM	β	LCI	UCI	LSM	β	LCI	UCI	LSM	β	LCI	UCI	LSM	β	LCI	UCI
PFOS in quartiles (ng/ml)																
Quartile 1 (1.50-3.85)	37.12	Reference			82.48	Reference			2.46	Reference			0.51	Reference		
Quartile 2 (3.85-5.20)	34.66	-2.46	-30.29	12.49	70.09	-12.39	-94.96	32.04	2.35	-0.11	-0.55	0.73	0.50	0.00	-0.09	0.12
Quartile 3 (5.20-7.25)	27.39	-9.73	-34.31	6.41	62.16	-20.32	-94.17	34.87	2.40	-0.06	-0.63	0.63	0.50	-0.01	-0.09	0.12
Quartile 4 (7.25-16.2)	13.14	-23.98	-47.12	-11.99	19.27	-63.21	-132.56	-26.72	3.78	1.33	0.17	1.82	0.50	-0.01	-0.12	0.09
p for trend	0.006				<0.001				0.017				0.988			
Q1 vs Q4 (p-value)	0.007				0.006				0.048				0.998			
PFOA in quartiles (ng/ml)																
Quartile 1 (<LOD-0.90)	17.85	Reference			33.12	Reference			3.48	Reference			0.58	Reference		
Quartile 2 (0.90-1.40)	24.51	6.66	-7.86	26.99	48.69	15.57	-23.96	74.84	2.79	-0.68	-1.31	0.17	0.51	-0.07	-0.16	0.05
Quartile 3 (1.40-2.20)	20.24	2.39	-16.85	16.43	29.82	-3.30	-46.26	41.97	3.05	-0.43	-1.26	0.40	0.45	-0.13	-0.20	0.03
Quartile 4 (2.20-5.30)	30.24	12.39	-7.23	34.41	67.43	34.32	-19.97	110.04	2.25	-1.23	-1.72	-0.25	0.48	-0.10	-0.19	0.03
p for trend	0.075				0.079				0.004				0.122			
Q1 vs Q4 (p-value)	0.272				0.284				0.042				0.350			

^a Fully adjusted for gestational age, maternal age, parity, smoking and caffeine intake during pregnancy, maternal educational level, and blood sampling period.

LOD: limit of detection

Table S5. Characteristics of mother-infant pairs in current analysis (n=185) compare with non-participants in this analysis (n=244) and participants in original cohort (n=429).

	Total (n=429)	Non-participants (n=244)	Participants (n= 185)
Characteristics	No. (%)/ mean ± SD	No. (%)/ mean ± SD	No. (%)/ mean ± SD
PFOS (median, 25-75 percentile)	5.2 (3.4-7.0)	5.2 (3.2-6.9)	5.2 (3.8-7.2)
PFOA (median, 25-75 percentile)	1.3 (0.8-1.8)	1.2 (0.7-1.6)	1.4 (0.9-2.2)
Maternal characteristics			
Age (years)	30.2 ± 4.7	30.5±4.8	29.7±4.7
Prepregnancy BMI (kg/m ²)	21.1 ± 3.0	21.2±3.2	21.0±2.9
Parity; primipara	202 (47.1)	103 (42.4)	99 (53.5)
Maternal educational level; ≤12 years	192 (44.7)	106 (43.4)	86 (46.5)
Annual income during pregnancy; <5 million yen	296 (69.4)	167 (68.7)	129 (70.5)
Smoking during pregnancy; yes	73 (17.0)	40 (16.4)	33 (17.8)
Alcohol intake during pregnancy; yes	129 (30.0)	69 (28.2)	60 (32.4)
Child characteristics			
Male infants	198 (46.1)	117 (47.9)	81 (43.8)
Gestational age (days)	275.4 ± 10.0	272.7±11.1	278.9±6.7